VII. Rejection of Claims 28-34

The Office Action rejected claims 28-34 under 35 U.S.C. section 112, second paragraph. Claims 28-34 have been cancelled, so the rejection is moot and should be withdrawn.

VIII. Conclusion

All issues raised by the Office Action have been addressed. Examination and allowance of claims 7, 9, 10, 15-17 and 37-38 is requested.

Respectfully Submitted,

Date: December 5, 2001

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CERTIFICATE OF EXPRESS MAIL UNDER 37 C.F.R. §1.10

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Date: December 5, 2001

Susan Bartholomew
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Susan Bartholomew
Signature of person mailing paper

PLEASE REPLACE PAGE ONE OF THE SPECIFICATION BY THE FOLLOWING UNMARKED PAGE

METHOD FOR TREATING CARDIAC MUSCLE DISORDERS BY ADMINISTRATION OF A BOTULINUM TOXIN

by

Stephen Donovan

BACKGROUND

The present invention relates to a method for treating cardiac muscle disorders. In particular, the present invention relates to a method for treating cardiac arrhythmia by administration of a neurotoxin to cardiac muscle.

The pumping action of the heart is controlled by sympathetic and parasympathetic (primarily vagal) nerves which abundantly innervate the heart. Heart rate can be increased by sympathetic stimulation and decreased by vagal stimulation. Additionally, many cardiac fibers, such as the sinus node (also called sinoatrial or SA node) have the capability of self-excitation. Stimulation of the sympathetic nerves causes release of norepinephine at the sympathetic nerve endings. Contrarily, stimulation of the parasympathetic nerves to the heart causes acetylcholine to be released at the vagal nerve endings. Hence, the parasympathetic nervous system is often referred to as a cholinergic system.

The release of acetylcholine by the postganglionic parasympathetic nerve endings, by acting upon the muscarinic receptors present in cardiac muscle tissue, as indicated, decreases the rate of rhythm of the sinus node and decreases the excitability of the AV junctional fibers between the atrial musculature and the AV node, thereby slowing transmission of the cardiac

impulse into the ventricles. The major site of action of parasympathetic control of the heart appears to be the sinoatrial node, where it reduces the heart rate in

VERSION OF PAGE ONE OF THE SPECIFICATION WITH MARKINGS TO SHOW THE CHANGES MADE

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The pumping action of the heart is controlled by sympathetic and parasympathetic (primarily vagal) nerves which abundantly innervate the heart. Heart rate can be increased by sympathetic stimulation and decreased by vagal stimulation. Additionally, many cardiac fibers, such as the sinus node (also called sinoatrial or SA node) have the capability of self-excitation. Stimulation of the sympathetic nerves causes release of norepinephine at the sympathetic nerve endings. Contrarily, stimulation of the parasympathetic nerves to the heart causes acetylcholine to be released at the vagal nerve endings. Hence, the parasympathetic nervous system is often referred to as a cholinergic system.

The release of acetylcholine by the postganglionic parasympathetic nerve endings, by acting upon the muscarinic receptors present in cardiac muscle tissue, as indicated, decreases the rate of rhythm of the sinus node and decreases the excitability of the AV junctional fibers between the atrial musculature and the AV node, thereby slowing transmission of the cardiac

impulse into the ventricles. The major site of action of parasympathetic control of the heart appears to be the sinoatrial node, where it reduces the heart rate in

UNMARKED VERSION OF THE CLAIMS

7. A method for treating bradycardia, the method comprising the step of intrapericardial injection of a botulinum toxin to a cardiac muscle, thereby treating bradycardia.

9. The method of claim 7, wherein the botulinum toxin inhibits formation or release of a neurotransmitter from neurons in the vicinity of the cardiac muscle.

10. The method of claim 9, wherein the neurotransmitter is acetylcholine.

15. The method of claim 7, wherein the botulinum toxin is botulinum toxin type A and the amount of botulinum toxin type A locally administered to the cardiac muscle is between about 0.01 U/kg and about 35 U/kg.

16. The method of claim 7 wherein the botulinum toxin is botulinum toxin type A and the amount of botulinum toxin type A locally administered to the cardiac muscle is between about 0.1 U/kg and about 30 U/kg.

17. The method of claim 7, wherein the botulinum toxin is botulinum toxin A and the amount of botulinum toxin A locally administered to the cardiac muscle is between about 1 U/kg and about 25 U/kg.

37. The method of claim 7, wherein the botulinum toxin is selected from the group consisting of botulinum toxins types A, B, C, D, E, F and G.

B4

38. A method for treating bradycardia, the method comprising the step of intrapericardial injection of a botulinum toxin type A to a cardiac muscle, thereby treating bradycardia.

sub D3 7

MARKED UP VERSION OF THE CLAIMS

7. A method for treating bradycardia~~a cardiac muscle disorder~~, the method comprising the step of ~~locally administering~~ intrapericardial injection of a ~~neurotoxin~~ botulinum toxin to a cardiac muscle, thereby treating ~~the cardiac muscle disorder~~ bradycardia.

Cancel claim 8.

9. The method of claim 7, wherein the ~~neurotoxin~~ botulinum toxin inhibits formation or release of a neurotransmitter from neurons in the vicinity of the cardiac muscle.

10. The method of claim 9, wherein the neurotransmitter is acetylcholine.

Cancel claim 11.

Cancel claim 14.

15. The method of claim 7, wherein the ~~neurotoxin~~ botulinum toxin is botulinum toxin type A and the amount of botulinum toxin type A locally administered to the cardiac muscle is between about 0.01 U/kg and about 35 U/kg.

16. The method of claim 7 wherein the ~~neurotoxin~~ botulinum toxin is botulinum toxin type A and the amount of botulinum toxin type A locally administered to the cardiac muscle is between about ~~0~~.1 U/kg and about 30 U/kg.

17. The method of claim 7, wherein the ~~neurotoxin~~ botulinum toxin is botulinum toxin A and the amount of botulinum toxin A locally administered to the cardiac muscle is between about 1 U/kg~~-~~ and about 25 U/kg.

Cancel claim 18.

Cancel claims 28-36.

Please add the following new claims:

37. The method of claim 7, wherein the botulinum toxin is selected from the group consisting of botulinum toxins types A, B, C, D, E, F and G.

38. A method for treating bradycardia, the method comprising the step of intrapericardial injection of a botulinum toxin type A to a cardiac muscle, thereby treating bradycardia.